THE HEMODYNAMIC BASIS OF ATHEROSCLEROSIS. FURTHER OBSERVATIONS: THE OSTIAL LESION

MEYER TEXON, M.D.

Department of Forensic Medicine
New York University Medical Center
Office of the Chief Medical Examiner of the City of New York
New York, N. Y.

INTRODUCTION

ATHEROSCLEROSIS may be considered as the reactive biological response of the arteries to the mechanical stresses generated by the flowing blood.[1-6]

This report analyzes the ostial or branch lesion by further correlating certain biological and mechanical properties of the circulatory system with special reference to intimal proliferation.[7, 8]

The vascular system has both biological and mechanical properties. Mechanically it serves as a conduit for the blood required by all body organs, its mechanical characteristics being determined by the physical structure and geometry of the blood vessels. The biological properties of the vascular system are those concerned with the cellular life processes of the blood vessels themselves: namely, their metabolic maintenance, growth, repair, and response to noxious stimuli, including mechanical stress.

STRESSES GENERATED BY FLOWING BLOOD

Physical or mechanical stress is defined as a force acting per unit area of surface. The stress at any point of a surface may be resolved into a normal component acting perpendicularly to the surface and a shear component acting parallel to the surface. Normal stresses (σ) may be either tensile or compressional depending on the direction of the force with respect to the reference surface. The effect of shear stress (τ) may

This study was supported in part by the Fan Fox and Leslie R. Samuels Foundation, New York, N. Y.; the Swift Newton Research Fund, New York, N. Y.; and the Dr. and Mrs. Henry Raphael Gold Research Fund, New York, N. Y.

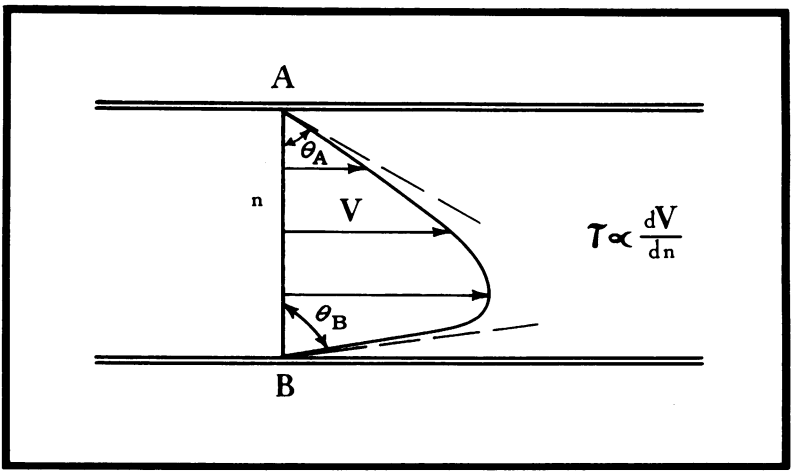

Fig. 1. In an unsymmetric velocity profile, the shear stress at the wall in 2-dimensional flow is greater at B than at A since the shear stress (τ) is proportional to the velocity gradient which is in turn proportional to the slope of the tangents to the velocity profile. As shown, $\theta_B > \theta_A$ and hence $\tau_B > \tau_A$.

produce either tensile or compressional stresses in the vessel wall, depending on the magnitude and direction of the shear stress. A specific stress component is characterized by its magnitude and direction with reference to a given surface. In contrast to steady flow, which characteristically produces a relatively constant compressional or tensile stress at a given site, pulsatile flow may be characterized by alternating compressional and tensile stresses at the same site. Turbulent flow may also be characterized by stresses occurring irregularly at a given site.

The hydraulic factors which are chiefly responsible for the development of normal stresses and shear stresses are the anatomical pattern (geometry of design) and the velocity distribution in the blood vessel. The shear stress at the wall depends on the velocity gradient at the interface. Hydraulic specifications, including velocity distribution or profile, in various vascular configurations can be analyzed more precisely in steady flow than in pulsatile or turbulent flow.[9] In all patterns of flow, however, a relative decrease in lateral pressure tends to develop at certain zones of predilection: namely, curvature, branching, bifurcation, tapering, and external attachment.[10] The decrease in lateral pressure may be related to a local increase in blood velocity. Also, increased

velocity will usually lead to an increase in shear stress at the interface. Shear stress in such instances may result in a tensile force in the vessel wall. In fact, shear stress, diminished lateral pressure, and tensile stress may be different expressions denoting coincidental forces at a given site.[11]

Shear stress at the wall of a blood vessel (Figure 1) is proportional to the rate of change of velocity in a direction normal to the wall.

The slope of the velocity profile away from the n axis is the value dV/dn which is related to the shear stress (τ) on the interface. The order of magnitude of the shear stress at the wall in small vessels may be estimated from Poiseuille's Law. For a vessel of diameter $D = 2$ mm., with a mean flow velocity $V = 3$ cm. per second and a viscosity $\mu = 4$ cp, the shear stress at the wall is

$$\tau = 8\ V\mu/d = 4.8 \text{ dynes/cm.}^2$$

Because of asymmetry, branches, and bends, it is possible for local shear stress to be several times the mean value.

The Ostial Lesion

Ostial lesion is the term applied to the intimal changes, including atherosclerotic plaques, which occur at the zone of origin of a branch vessel. These lesions are here interpreted as the local biological response of the blood vessel to hydraulic forces generated by the flowing blood. Although the patterns of flow at a branch necessarily vary because of variations in pulsatile flow as well as variations in geometry or anatomical design, idealized situations may be analyzed precisely and may serve as a basis for interpreting more complex patterns of flow. The distribution of the pathological changes reflects the predominant pattern of flow as well as the change in pattern of flow due to the progressively developing anatomical lesion itself. The atherosclerotic plaque is, in effect, the composite result of all the pertinent hydraulic conditions. These may include pulse rate, stroke volume, rhythm, amplitude, elasticity, ratio of the diameter of the main stem to branch diameter, shape of the ostial orifice, angle of branching, and velocity of flow.

The laws of fluid mechanics determine that the pattern of flow at the site of a branch is usually characterized by several zones of diminished lateral pressure. These may be identified at points D_1 and D_2 (see Figure 2). The relatively high shear stress at point F reflects the in-

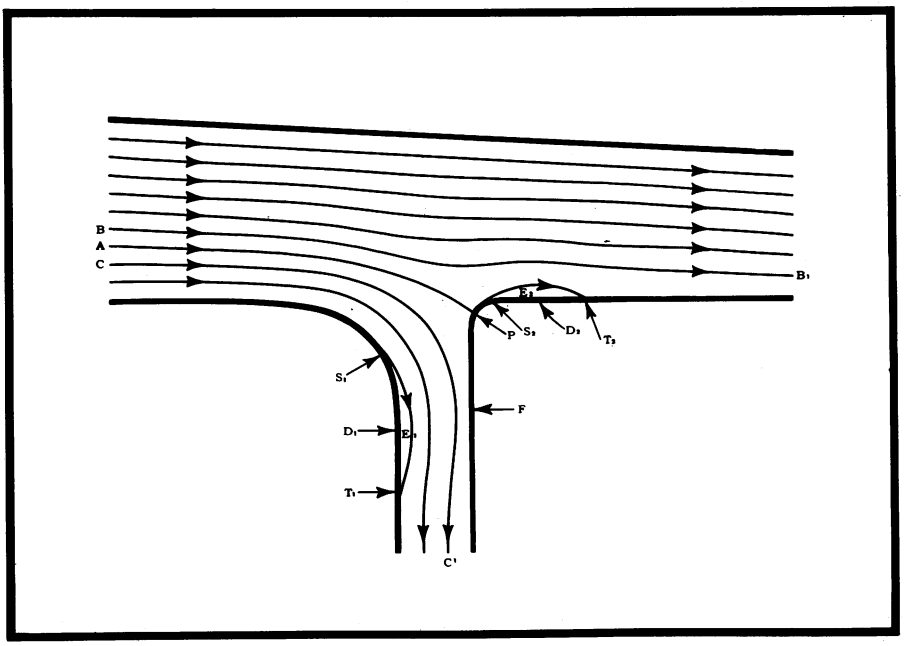

Fig. 2. A qualitative sketch of streamlines expected where a small blood vessel (say 2 mm. diameter) leaves a larger blood vessel (say 4 mm. diameter) at right angles.

At the stagnation point P, the shear stress is zero and the pressure will be a local maximum.

The dividing streamline is AP; fluid above AP, such as BB′ remains in the parent vessel; fluid below AP, such as CC′, enters the daughter vessel.

At the point S_1, a separation may occur and result in the formation of the eddy E_1. The pressure at D_1 will be at slightly lowered pressure due to the curvature of the streamline S_1T_1.

Similarly, there may be a second eddy E_2 with a separation point S_2 and a slightly lowered pressure point D_2 due to the curvature of the streamline S_2T_2.

The point F may suffer a relatively high shear stress because of the higher velocity gradient there.

creased velocity gradient adjacent to the wall surface or at the interface.

It is notable that in any branching anatomical pattern a stagnation point must develop at the distal margin of the ostial orifice. The stagnation point is a point of high pressure and theoretically zero velocity (and zero shear stress), and is singularly free of atherosclerotic change. Because of the geometry in some cases, the streamlines of flow are forced to curve downstream from the stagnation point, giving rise to a local zone of increased velocity and probably lower pressure at point D_2 (see

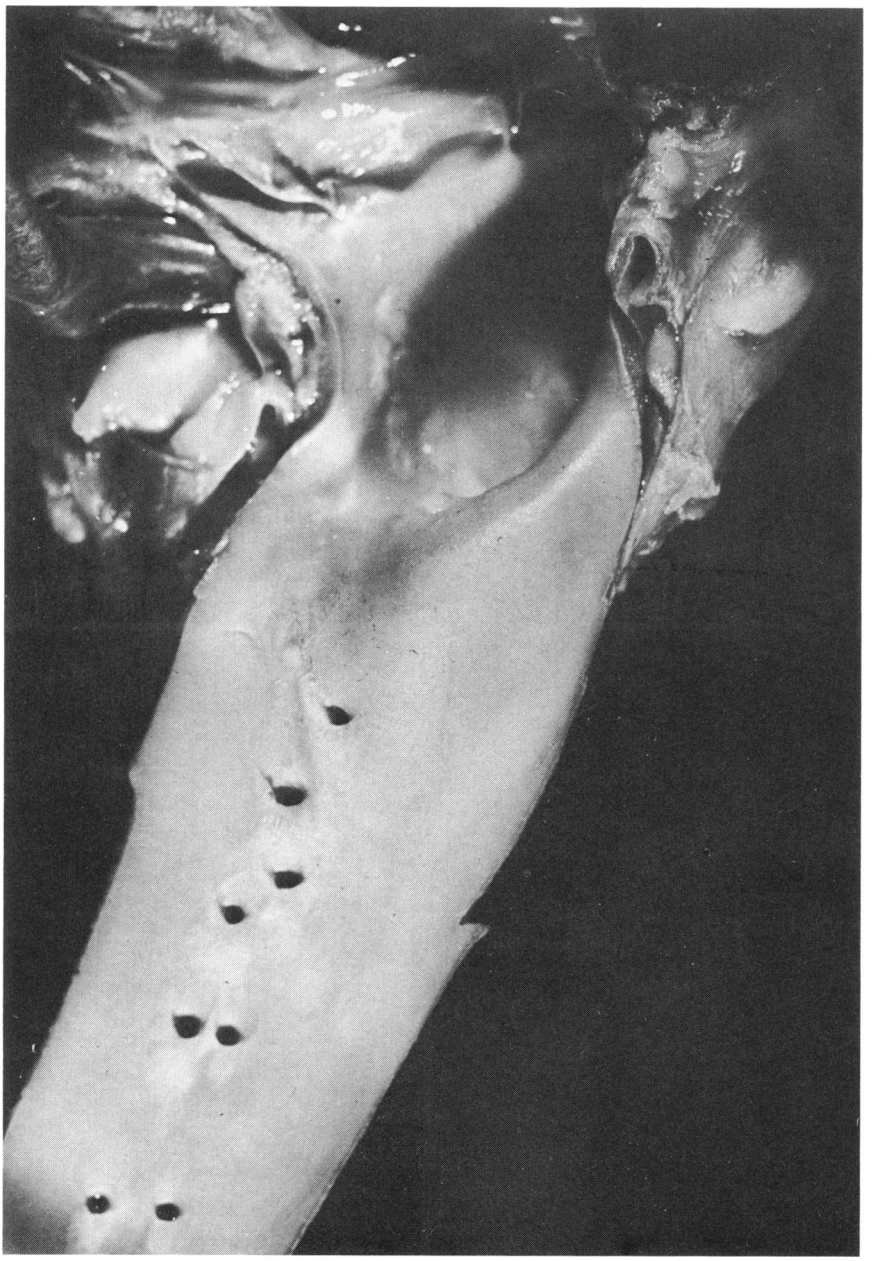

Fig. 4. Ostial lesions in dorsal aorta (dog). Normal diet. Note atherosclerotic plaques distal to orifices of intercostal arteries.

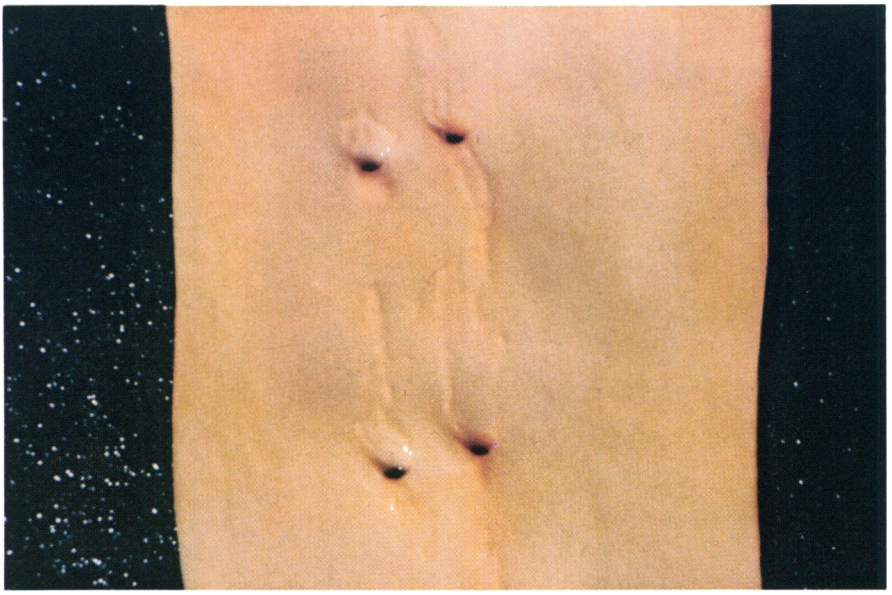

Fig. 3.

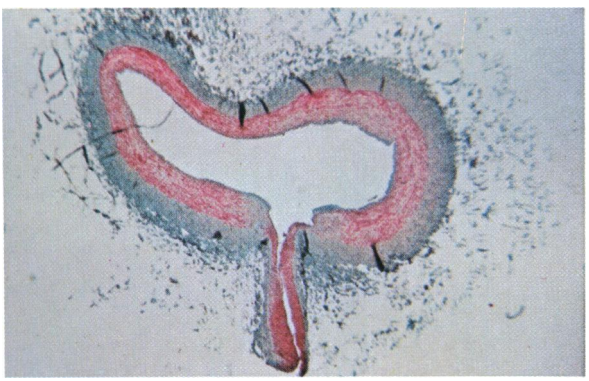

Fig. 5A.

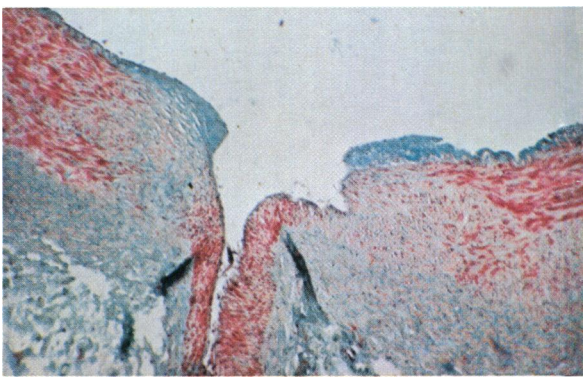

Fig. 5B.

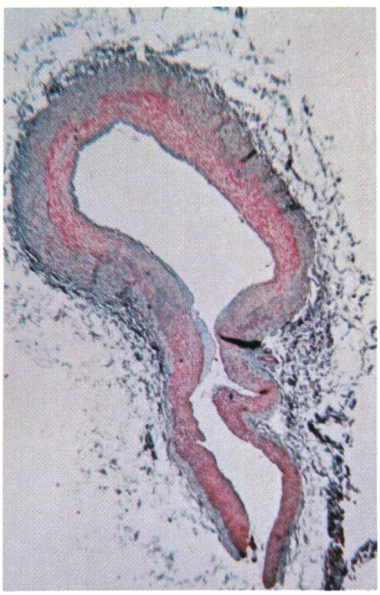

Fig. 5C.

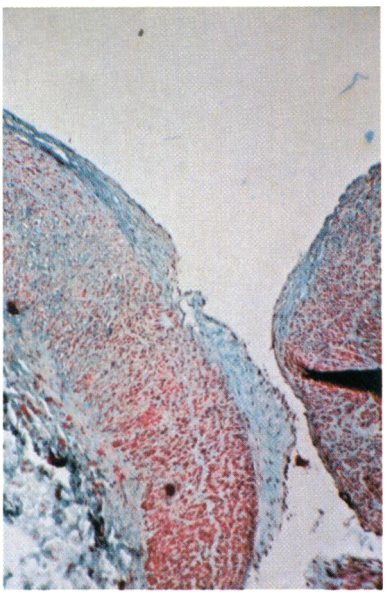

Fig. 5D.

Figure 2). A characteristic V-shaped lesion in the main stem distal to the branch is the localized biological or reparative response to this flow pattern (Figures 3 and 4).

The pattern of blood flow into the orifice of a branch normal to the direction of main flow may produce, in effect, a tensile or suction force upon the wall (Figure 5).

Comment

Zones of branching give rise to ostial lesions. They are examples of sites of predilection for atherosclerosis—localized areas of diminished pressure where the endothelium is exposed to the lifting or pulling effect and shear stress exerted by the flowing blood. This is the initial stimulus. The initial response is a biological change, a reparative or reactive thickening due to the proliferation of intimal cells. There is no evidence of cellular reaction, lipid change, or vascularization in the early stage of intimal thickening. The internal elastic layer appears to remain intact and unchanged in the early lesions.[7, 10]

With continuing blood flow, the thickening intima encroaches upon the lumen. The plaque progresses in size, shape, and degree, further pathological change depending upon the pattern of blood flow and the zones of varying diminution in lateral pressure. The pathological process may also be the biological response to the increased shear stress at the wall. The varying successive hydraulic stresses may be reflected in the orientation of cells in successive layers of fibroblastic proliferation. Cellular elements and lipids are added to the intimal and fibroblastic proliferation as part of the pathological response in situ, while fibroblastic proliferation appears to be the dominant pathological change at all stages.

Fig. 3. Ostial lesions—Atherosclerotic plaques in dorsal aorta (human) distal to origin of intercostal arteries—the localized biological response to the local pattern of blood flow which produces the localized low pressure zone. Note other linear atherosclerotic plaques on the posterior wall (attachment lesions).[4, 10]

Fig. 5. Cross sections normal to axis of femoral artery (dog). Typical ostial lesions are observed at the junction of the parent vessel with a branch. These lesions may also be associated with a separated flow which occurs early in systole when velocity of flow in the parent vessel is first increasing rapidly.

Summary

The influences of fluid mechanics are reviewed with special reference to patterns of flow in the region of the orifice of a branching blood vessel. The traumatic (pathological) effects are associated with zones of low pressure, zones of increased shear stress, and increased velocity gradient. Intimal proliferation associated with an ostial orifice is demonstrated to be the biological response to the tensile stress created by the flowing blood at low pressure zones determined by the anatomical pattern. The ostial lesion is here interpreted to be the biological response of the blood vessels to the mechanical stimulus (diminished lateral pressure) inherent in the effect of the laws of hemodynamics[12] as they apply to local hydraulic specifications in the zone of origin of a branch vessel.

REFERENCES

1. Texon, M.: A hemodynamic concept of atherosclerosis with particular reference to coronary occlusion. *Arch. Intern. Med. 99*:418-27, 1957.
2. Texon, M.: The hemodynamic concept of atherosclerosis. *Bull. N. Y. Acad. Med. 36*:263-74, 1960.
3. Texon, M.: The Role of Vascular Hemodynamics in the Development of Atherosclerosis. In: *Atherosclerosis and its Origin,* Sandler, M. and Bourne, G. H., editors. New York, Academic Press, 1963, p. 167.
4. Texon, M., Imparato, A. M. and Helpern, M.: The role of vascular dynamics in the development of atherosclerosis. *J.A.M.A. 194*:1226-30, 1965.
5. Gyurko, G. and Szabo, M.: Experimental investigations of the role of hemodynamic factors in formation of intimal changes. *Surgery 66*:871-74, 1969.
6. Reemtsma, K., Sandberg, L. B. and Greenfield, H. H.: Some theoretic aspects of vascular degeneration. *Amer. J. Surg. 119*:548-52, 1970.
7. Texon, M., Imparato, A. M., Lord, J. W. and Helpern, M.: The experimental production of arterial lesions: Furthering the hemodynamic concept of atherosclerosis. *Arch. Intern. Med. 110*:50-52, 1962.
8. Imparato, A. M., Lord, J. W., Texon M. and Helpern, M.: Experimental atherosclerosis produced by alteration of blood vessel configuration. *Surg. Forum 12*:245-47, 1961.
9. McDonald, D. A.: *Blood Flow in Arteries.* Baltimore, Williams & Wilkins, 1960.
10. Texon, M.: Mechanical Factors Involved in Atherosclerosis. In: *Atherosclerotic Vascular Disease,* Brest, A. N. and Moyer, J. H., editors. New York, Appleton-Century-Crofts, 1967, pp. 23-42.
11. Fry, D. L.: Certain chemorheologic considerations regarding the blood vascular interface with particular reference to coronary artery disease. *Circulation* (Suppl.) *39* and *40*:39-59, 1969.
12. Texon, M.: The Role of Vascular Dynamics (Mechanical Factors) in the Development of Atherosclerosis. In: *Coronary Heart Disease,* Russek, H. I. and Zohman, B. L., editors. Philadelphia, Lippincott, 1971, pp. 121-36.